The Benefit of Japanese Patent Law System Over that of the US in the Pharmaceutical Area

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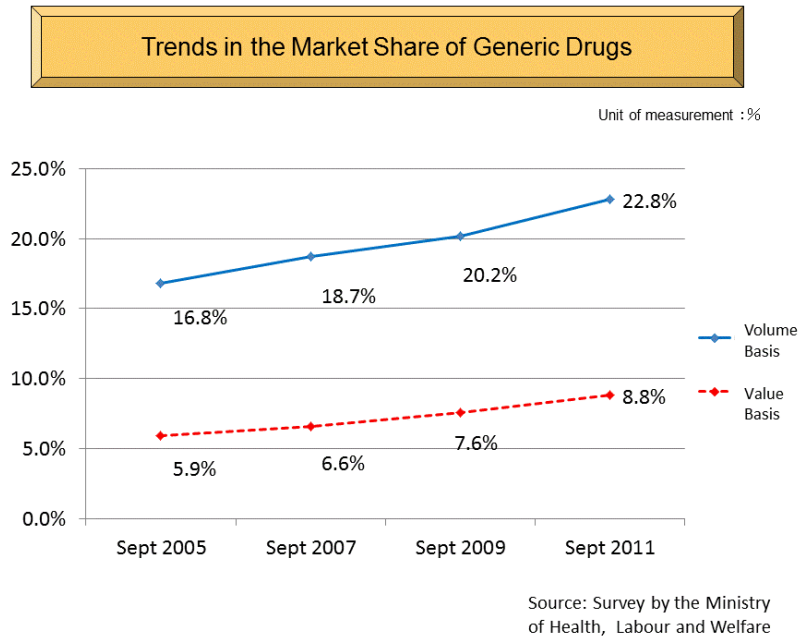
Discover IP JAPAN
Conference 2017

- Japan undeniably second largest pharmaceutical market after US
- Due to aging population and attendant increase in healthcare cost, Japanese government started to aggressively promote the use of generic drug since 2007



Source: Survey by the Ministry of Health, Labour and Welfare

- More numbers:
  - 2016 – about 60% (by volume)
  - Japanese government wants to increase the use to 80% in fiscal year 2018-2020!

- Patents are only tools available to prevent market erosion for pharmaceutical companies
  - The opportunity cost of not filing patents in Japan, or “not doing things right” in Japan could be enormous

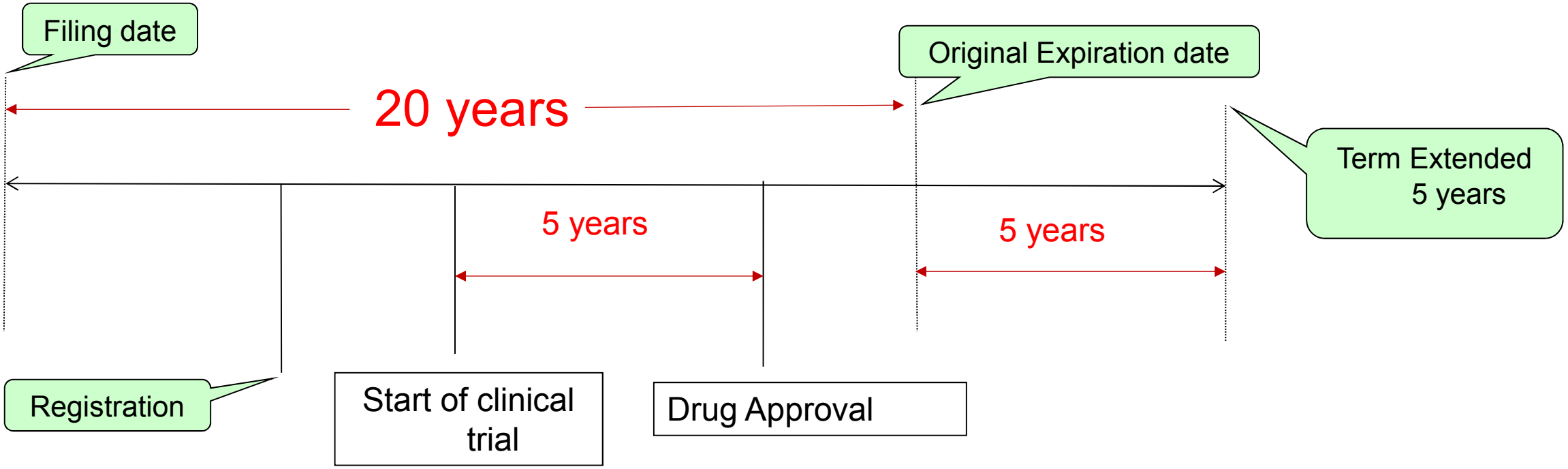
Comparison Between US v Japanese Patent Term Extension System

- Both Japan and US enjoys up to 5 years on top of normal 20 years if a drug undergoes clinical and regulatory approval period
  - However there are few major differences between the two systems overall favorable in the Japanese system

- Japanese Patent Law Article 67 (2): Where there is a period during which the patented invention is unable to be worked because approvals prescribed … to ensure the safety (i.e. of pharmaceutical and agricultural products)…, patent right may be extended … by a period not exceeding 5 years.

- US Patent Law 35 USC § 156 (paraphrased): Up to five years of extension for (1) ½ of IND period and full review period; but (2) total period of remaining patent term including the extension cannot exceed 14 years from approval; and (3) only one patent extension for one product (active ingredient).

Outline of the Japanese PTE system

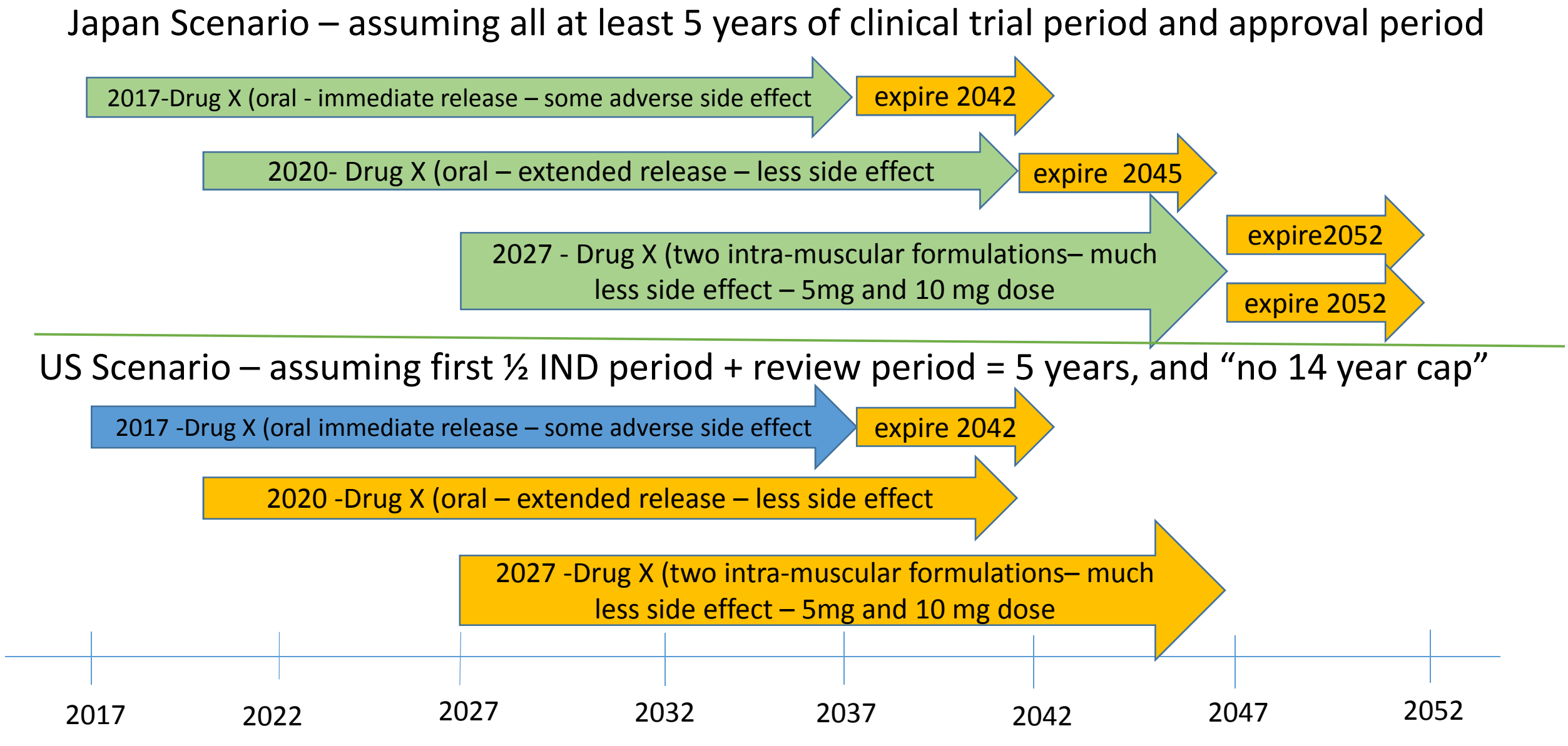


Applicable for drugs for humans and animals, and agricultural chemicals

- Japan – Full 5 years for clinical trial and approval delay if such is 5 years. No limitation of ½ of IND period or “14 year cap”; and more importantly many patent extensions on one product (new formulation, new use, new dosage, etc)

Japan	US
Full 5 years	Under 5 years
- No ½ of IND period	- ½ of IND period
- No 14 year cap from approval	- 14 year cap from approval
Allows multiple PTEs for one (formulation, dose, new uses, etc)	Only one PTE per drug

Hypothetical Anti-arthritic Drug X



Expert Opinion on Therapeutic Patents
ISSN: 1354-3776 (Print) 1744-7674 (Online) Journal (2016)

Strategic balance of drug lifecycle management options differs between domestic and foreign companies in Japan

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"…Some foreign companies have development departments in Japan that conduct drug approval procedures, while they have intellectual departments in other countries that conduct patent prosecution through patent agents in Japan; that is, intellectual departments and development departments within a company being in different countries might cause a lack of cooperation among those departments and bring difficulty in coordinating patent prosecution schedules and drug approval schedules for successful PTEs. Because domestic companies usually have intellectual departments and development departments in Japan, departments of domestic companies generally have fewer obstacles to cooperation than do foreign companies."

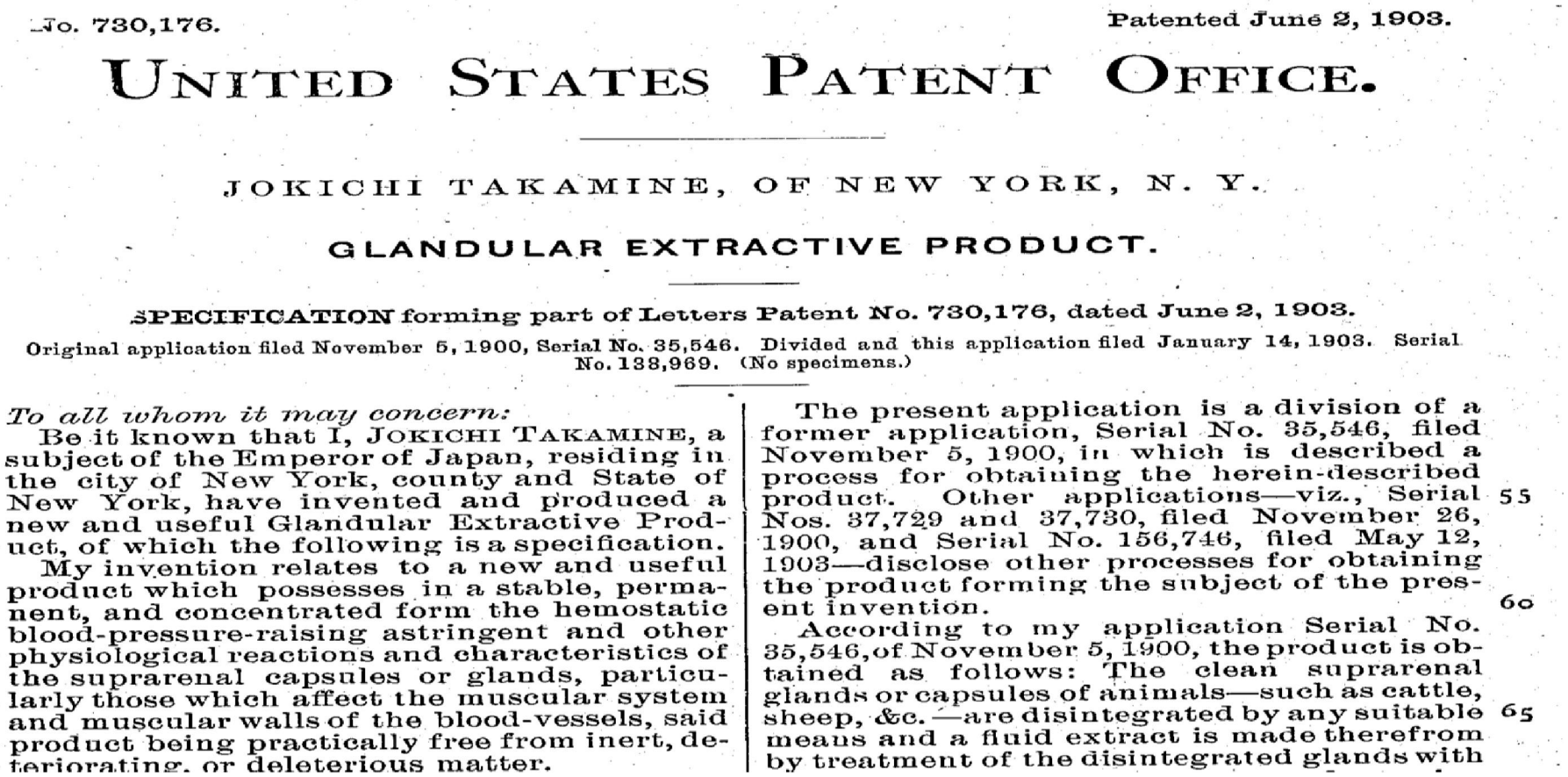
How best to maximize JP PTE

- Both US and Japan - need to have patent issued as early as possible.
  - Some years back in Japan, 7 years from filing to request examination was permitted
    - The applicant in the article was not familiar with JP PTE system; took time to obtain patent 10 years after filing which caused patent issued after drug approval
  - Today request for exam needs to be made after 3 years, but consult with you JP attorney if even accelerated examination is preferred
  - One many not know that JP allows multiple extensions on one product; let alone one can and needs to extend every forms (e.g. different dosages)
  - Mistakes cost the two companies heavily and allowed early entry of generics

- Do not be disadvantaged by being non-Japanese companies:
  - Early and tight communication between Japanese agents absolute must
  - Like before going to doctor, learn about your illness so you can ask educated questions
  - Create JP country specialist

Current Risks Affecting Pharmaceutical, Diagnostic, and Nutraceutical Companies in the US

- Since 19th century US patent office granted patents on products found in nature isolated by man
- US730176 - adrenaline "practically free from…associated gland tissue" (issued 1903)



No. 730,176. Patented June 2, 1903.

UNITED STATES PATENT OFFICE.

JOKICHI TAKAMINE, OF NEW YORK, N. Y.

GLANDULAR EXTRACTIVE PRODUCT.

SPECIFICATION forming part of Letters Patent No. 730,176, dated June 2, 1903.

Original application filed November 5, 1900, Serial No. 35,546. Divided and this application filed January 14, 1903. Serial No. 138,969. (No specimens.)

To all whom it may concern:

Be it known that I, JOKICHI TAKAMINE, a subject of the Emperor of Japan, residing in the city of New York, county and State of New York, have invented and produced a new and useful Glandular Extractive Product, of which the following is a specification.

My invention relates to a new and useful product which possesses in a stable, permanent, and concentrated form the hemostatic blood-pressure-raising astringent and other physiological reactions and characteristics of the suprarenal capsules or glands, particularly those which affect the muscular system and muscular walls of the blood-vessels, said product being practically free from inert, deteriorating, or deleterious matter.

The present application is a division of a former application, Serial No. 35,546, filed November 5, 1900, in which is described a process for obtaining the herein-described product. Other applications—viz., Serial Nos. 37,729 and 37,730, filed November 26, 1900, and Serial No. 156,746, filed May 12, 1903—disclose other processes for obtaining the product forming the subject of the present invention.

According to my application Serial No. 35,546, of November 5, 1900, the product is obtained as follows: The clean suprarenal glands or capsules of animals—such as cattle, sheep, &c.—are disintegrated by any suitable means and a fluid extract is made therefrom by treatment of the disintegrated glands with

- US2449866 – claim 13: streptomycin (issued 1948)

Current Risks Affecting Pharmaceutical Industry, Diagnostic, and Nutraceutical Companies in the US

- Also issued patents on diagnostic methods of human diseases

- But dramatic changes started to occur since around early 2010;
  - Patent eligibility on important pharmaceutical assets now cast into question
    - Proteins, antibiotics, and other pharmaceutically active agents found, and isolated from nature intended to be developed as medicines
    - Innovative diagnostic methods (e.g personalized medicines) for predicting and/or diagnosing autism, cancer, schizophrenia…

  - *Mayo v Prometheus* (method of optimizing drug treatment; Supreme Court, 2012);
  - *ACLU v Myriad (human genes;* Supreme Court, 2013)
  - *Sequenom v Ariosa* (genetic diagnostics; CAFC 2015, *cert denied*)

  - The enforceability of already issued patents not clear

  - Already affecting in-licensing, patent filings and maintenance activities

ACLU v Myriad

- U of Utah isolated BRAC1/2 genes, and discovered mutated forms are associated with ovarian and breast cancer

- Filed patent on isolated DNA encoding BRAC1/2 (mutated and wildtype) genes

- U.S. 5747282 for BRCA 2
  1. An isolated DNA molecule coding for a BRCA2 polypeptide…of SEQ ID NO:2.
  6. An isolated DNA molecule coding for a mutated form of the BRCA2 polypeptide set forth in SEQ ID NO:2, wherein said mutated form of the BRCA2 polypeptide is associated with susceptibility to cancer.

- U.S. 5837492 for BRCA 1
  1. An isolated DNA comprising an altered BRCA1 DNA…

US Supreme Court in *Myriad*

- *"We merely hold that genes and the information they encode are not patent eligible under § 101 simply because they have been isolated from the surrounding genetic material."*
  - The main argument focused that claims of BRCA1/2 genes are more informational than composition of matter

- Isolated DNA not patent subject matter under § 101, unless it is significantly different from found in nature. (applied the analysis adopted by Mayo)
  - cDNA is patentable because it not naturally occurring.

- **35 U.S.C. § 101 INVENTIONS PATENTABLE.**

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter….. may obtain a patent…

- Until about 2012, courts have always maintained "judicial exceptions" of (a) pure laws of nature, (b) natural phenomenon, and (c) abstract idea not patentable, but their application patentable.
- *Diamond v Chakrabarty,* (Supreme Court, 1980) – "anything under the sun that is made by man"

Examination Guideline JP vs US

USPTO Interim Guidance on Subject Matter Eligibility

(https://www.uspto.gov/patent/laws-and-regulations/examination-policy/2014-interim-guidance-subject-matter-eligibility-0)

- Dec 2014, Nature–Based Product Examination Guideline
  - Antibiotic L (protein) – not patent eligible
  - Purified antibodtic L – patent eligible (if when purified takes different form)

Japanese Patent Law

- Article 29 (1) … an invention that is industrially applicable may be entitled … a patent....
- Article 2, paragraph 1 defines invention as "the highly advanced creation of technical ideas by which a law of nature is utilized".

Japanese Examination Guideline

  - Invention does not include simple “natural law” or “simple observation” (same as US)
  - But invention include chemical products, micro-organisms, etc. which are isolated by man from nature

- US 5747282 (BRCA1) – JP3241736; and
- US 5837492 (BRCA2) – JP3455228

- US6033857 (BRCA2) - claim 2 declared not patent eligible by CAFC
  - Claim 2. A method of diagnosing a predisposition for breast cancer…comparing germline sequence of BRAC2 from subject with the wildtype… wherein alteration…indicates a predisposition to said cancer

- JP3399539
  - Claim 1 – A method to identify the presence of breast and ovarian cancer gene in an individual by comparing BRCA1 gene from the individual to that of the wildtype wherein alteration indicates the presence of the cancer gene

- JPO Examination Guideline (10/2015) – patent eligible
  - Example 5: A method of examining the susceptibility of the examinee to hypertension by determining the type of base …in X gene…and comparing…with standard

What About Personalized Diagnostic Methods?

- Until recently, fetal chromosomal abnormalities detected by highly invasive amniocentesis and villus chorionic assays, which involved high risk to the fetus.
- Drs Lo (CN) and Wainscoat (GB) developed innovative non-invasive method of detecting cffDNA in mother's serum/plasma. Filed patent (US625840) assigned to ISIS.
- Sequenom commercializes MATERNIT21® under license from ISIS using cffDNA; Ariosa launched competing method named HARMONY™
- In *Ariosa v Sequenom* (Fed Circuit 2015)
  - CAFC ruled that certain methods claimed in US6258540 patent ineligible
    - Claim1. Amplifyng paternally inherited DNA from plasma or serum from pregnant female; and (2) detecting the presence of such DNA of fetal origin
- Sequenom could not block entry of HARMONY. Now at least three players using this method in US.

Reason behind CAFC's decision

- Claims are directed to natural phenomenon (the presence of paternally inherited cffDNA in maternal blood/serum), and recited steps of amplifying and detecting cffDNA are routine methods

- Applied analysis of *Mayo*
  - First determine if claim is directed to patent ineligible concept (law of nature, natural phenomenon, or abstract ideas), if so, if significantly more is added to the claim.
  - Judge Dye in denying hearing en banc" said the claims might be patentable if "narrow in scope" otherwise they are overbroad

- JP4245666 – Patent still alive, and clinical trial on the technology started 2016

- Study conducted by Bernard Chao of U of Denver reported that 15.9% of patent applications related to judicial exceptions received rejections before *Mayo* (another US Supreme Court case of) but 86.4% rejection after *Mayo* in Art Unit 1634 (other units not considered which also receives personalized medicine applications)

Another Attack under § 101

- In 2017, the District of Delaware will address Merck's § 101 challenge (BMS v Merck) to three Ono Pharma patents claiming methods of treating cancers using anti-PD1 antibodies
  - eg US9067999

    1. A method of treating a lung cancer comprising administering a composition comprising a human or humanized anti-PD-1 monoclonal antibody…

- In April 2016, Delaware court accepted Merck's argument that the claims were directed to the natural phenomenon of using T cells to activate the immune system, thereby satisfying the first prong of § 101 analysis under *Mayo*
  - Second prong of whether claims "add enough" beyond the natural phenomenon will be addressed in early 2017

- Are some US companies cutting back on filings, or at least giving up prosecutions easily upon receiving rejections?
  - In the US, biologic drugs enjoys 12 years of market exclusivity.
  - Japan only 8 years of re-examination period (i.e. market exclusivity).
- Even if in the one decides to forego US filing or maintenance, keep the case alive in Japan. The outcome is better than that of US.
  - Ono Pharma's JP equivalents intact
  - File US priority case (even provisionals), and use those to claim priority in Japan
  - Some tendencies to start with narrower claims in the US directed to some biological inventions (in fear of file wrapper estoppel), but do not so at such early stage in Japan. Once again, maintain tight contact with your Japanese patent attorneys